OPEN ACCESS

University of BRISTOL

England, C. Y., Moss, L., Beasley, M., Haupt-Schott, I., Herbert, G., & Atkinson, C. (2019). A survey of UK centres on low iodine diet recommendations prior to radioiodine ablation therapy for differentiated thyroid cancer. *European Thyroid Journal*. https://doi.org/10.1159/000504706

Peer reviewed version

Link to published version (if available):
10.1159/000504706

Link to publication record in Explore Bristol Research
PDF-document

This is the author accepted manuscript (AAM). The final published version (version of record) is available online via Karger Publishers at https://www.karger.com/Article/Abstract/504706 . Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research
General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available:
http://www.bristol.ac.uk/red/research-policy/pure/user-guides/ebr-terms/

A survey of UK centres on low iodine diet recommendations prior to radioiodine ablation therapy for differentiated thyroid cancer

Clare Yvonne England[1,2*], Laura Moss[3], Matthew Beasley[4], Ingrid Haupt-Schott[3], Georgia Herbert[1], Charlotte Atkinson[1]

[1]National Institute for Health Research Bristol Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, UK
[2]Centre for Exercise Nutrition and Health Sciences, School for Policy Studies, University of Bristol, Bristol, UK
[3]Velindre Cancer Centre, Velindre Road, Whitchurch, Cardiff, UK
[4]University Hospitals Bristol NHS Trust, Marlborough Street, Bristol, UK

Running title: Low iodine diet 2019 survey

Corresponding author

Clare Yvonne England

Centre for Exercise, Nutrition and Health Science, School for Policy Studies, University of Bristol

8 Priory Road

Bristol

Tel: 0117 342 1759 or 0117 331 0573

e-mail: clare.england@bristol.ac.uk

Keywords: Thyroid cancer; low iodine diet; radioiodine ablation; survey

Abstract

Background: Guidelines suggest that a low iodine diet (LID) is advised prior to radioiodine ablation (RIA) for thyroid cancer. We aim to describe current practice regarding LID advice in the UK, determine uptake of the 2016 UK LID Working Group diet sheet and discover whether there are differences in practice. ***Methods:*** Online survey distributed between November 2018-April 2019 to centres in the UK that administer 131I. We asked questions on whether a LID is advised, for how long, how advice is presented, whether and how compliance is measured and whether treatment is delayed if LID advice is not followed. ***Results:*** Fifty-six clinicians from 47 centres that carry out RIA for thyroid cancer responded. Forty-four centres (94%) advise a LID prior to RIA, the majority for 14 days (82%). Two-thirds of centres use the UK LID Working Group diet sheet. Patients are told to resume normal eating when 131I is administered at 17 (39%) centres, with 18 (41%) advising waiting for 24-48 hours after administration. Most centres (95%) use only a simple question or do not assess compliance. Only 2 (5%) indicate that RIA would be delayed if someone said they had not followed LID advice. ***Conclusions:*** UK practice regarding the LID prior to RIA for thyroid cancer is consistent with current guidelines but non-adherence does not usually delay RIA. The UK Low Iodine Diet Working Group diet sheet is widely recognised and used. Practice could be improved by centres working to harmonise advice on when to restart a normal diet.

250 words

Background

Thyroid cancer accounts for less than 1% of cancer cases in the UK. However, incidence is increasing and between 2014 to 2016 there were an average of 3527 new cases of thyroid cancer annually in the UK, compared to 1125 in 1993(1, 2). Differentiated thyroid cancer accounts for 95% of cases. The prognosis for differentiated thyroid cancer is good, 10-year survival rate is 80-90%, although recurrence or persistent disease is estimated to occur in 10-30% of cases(3), with rates as high as 68% observed in high risk patients(4). Treatment is often total thyroidectomy, followed by radioiodine remnant ablation with ^{131}I (RIA) to destroy thyroid tissue remaining post-surgery(5). High iodine status can interfere with uptake of ^{131}I. The UK Guidelines for the management of thyroid cancer state that, based on expert opinion, exposure to iodinated contrast and treatment with drugs or supplements high in iodine should be avoided, and people should be advised to follow a low iodine diet (LID) of 1-2 weeks, prior to RIA(5). There is, however, mixed evidence on whether LIDs impact on ablation success(6), particularly in countries with generally low iodine intakes such as the UK(7).

Two reviews have been conducted, one systematic(8), one narrative(6), examining the use of LIDs prior to RIA. Randomised controlled trials indicate that advice to follow a LID for 1-2 weeks reduces urinary iodine. However, evidence that LID advice improves ablation success comes only from retrospective studies and is inconclusive. A study in the Netherlands(9) compared people who followed a LID for 7-days and reduced 24-hour urinary iodine excretion to <50mcg/day with historic controls given no dietary advice. Those following a LID experienced 65% success rate vs 48% for controls ($p<0.001$). A study in Korea(10) found only excessive iodine intake, measured as a urinary iodine creatinine ratio (UI/Cr) >250mcg/gCr, to be associated with increased odds of unsuccessful ablation (OR: 4.74, 95% CI: 1.78–12.63). Three other retrospective studies, in the USA(11) and Korea(12, 13) have found no difference in ablation success rates between cohorts that were advised a 10-14 day LID and historic controls who were given no advice(11); no difference between people following a very restrictive 2-week LID vs those following a less restrictive 2-week LID(12); and no difference in either ablation success or spot urine iodine concentration (UIC) between people following a 1-week vs those following a 2-week LID(13).

Despite the mixed evidence, the European Association of Nuclear Medicine Therapy Committee recommends that RIA should be postponed if UIC is >150-200mcg/l(3) and that clinicians should aim for a UIC <100mcg/l or a UI/Cr of <100mcg/gCr, with optional LID advice. UK guidelines do not give details on the level of iodine restriction necessary to achieve a UI/Cr of <100mcg/gCr, whereas American Thyroid Association guidelines advise restricting iodine intake to <50mcg/day(6). In contrast, in Korea, where intakes of iodine are much higher than in the UK and USA, guidelines are to restrict iodine intake to <100mcg/d. Italian guidelines do not advise an LID at all prior to RIA(14).

In the 2000s, there were anecdotal reports in the UK that there were variations in practice and patients were finding LID advice confusing(15). Consequently, the UK Low Iodine Diet Working Group (UK LID-WG) developed a UK LID diet sheet(16) and initially distributed it in 2016 (supplement). It is uncertain how widespread use of the diet sheet is and, given the lack of robust evidence that a LID affects ablation success and that international guidelines differ, it is possible that practice within the UK still varies.

This study was a survey of current practice regarding advice on LIDs prior to RIA in the UK. The aims were to determine whether practice varies across different centres, whether the UK LID-WG diet sheet is in use (and if not, why not) and to discover whether centres monitor compliance with a LID and if treatment is delayed if a LID is not followed.

Methods

A short electronic survey was designed on Online Surveys (Jisc, UK) for distribution to centres in the UK that administer ^{131}I for people undergoing treatment for thyroid cancer. The survey included 10 main questions, with a maximum of 20 follow-ups. Questions were a mixture of multiple choice with some free text boxes and included questions on how well clinicians thought patients coped with the diet (supplement). The survey could be completed anonymously, although at the end people were asked to identify their centre. Participation in the survey was voluntary, with informed consent assumed through completion.

There is no national list of centres that administer radioiodine in the UK. A list of possible centres was created from information held by the UK LID-WG, the Internal Dosimetry Users Group and through the authors' clinical networks. A brief invitation e-mail containing a link to the questionnaire and an explanation of the purpose of the survey was sent to identified centres in November 2018 and up to three reminders were sent between January 2019-April 2019. Practice regarding who prescribes and administers RIA varies in the UK, so e-mail addresses of clinicians known personally to the authors or listed on hospital websites were used or e-mails were sent to Nuclear Medicine or radiology department addresses. The e-mail included the contact details of two of the authors (CE and LM) so that recipients could find out more details or request no further contact. Information and a link to the survey was also distributed at a Thyroid Cancer Study day held at the Royal Marsden Hospital, London in December 2018. In April 2019 follow up e-mails were sent to hospitals in regions that appeared to have low coverage.

Responses were collated and are presented descriptively. Qualitative free text responses were summarised.

Results

Sixty-four hospitals were contacted, and responses were received from 53 (83%). Six hospitals (9%) indicated that they were not centres for RIA for thyroid cancer. Clinicians from 47 centres administering RIA (73%) completed the survey. For seven centres two responses were received and for one centre there were three responses, giving a total of 56 responses. Overall, national coverage was good (table 1). Responses were received from radiologists and nuclear medicine specialists (physicists and nurses) (n=15), other clinical nurse specialists (n=12), clinical scientists (n=12), oncologists (n=8), nuclear medicine consultants (n=3), unspecified consultants (n=4), one endocrinologist and one dietitian.

The mean estimated number of people treated with radioiodine for thyroid cancer at each centre/year was 46 (SD 28), giving a total estimated number of people treated of 2182 annually. The minimum number treated per centre was estimated to be 10 people, the maximum 150.

Three centres did not routinely advise a LID prior to RIA for all people. Of these, one small centre (treating approximately 10 people/year) indicated that they were not aware of the guidelines and another (treating approximately 80 people/year) indicated that there was no evidence for effectiveness. The remaining centre (treating approximately 40 people/year) responded that the provision of LID advice varied by clinician and it was more common not to advise the diet. Another centre also indicated that advice to follow a LID varied by clinician, one centre advised a LID for only 2 days prior to RIA, all others advised restriction for 1-2 weeks, as per the guidelines.

Table 2 summarises survey answers from the 44 centres who indicated that they advised people to follow a LID. For some questionnaire items, different responses were provided by different clinicians from the same centre, indicated in the table.

Most centres (66%) reported using the UK LID-WG diet sheet. Of those who did not, four (9%) were not aware of the working group suggestions and clinicians from four centres (9%) thought it was too restrictive, one of whom specifically said they did not advise people to restrict dairy products as much.

People were instructed to resume a normal diet immediately after taking ^{131}I at 17 (39%) centres, 2 hours after taking the RIA capsule by one centre and 24-48 hours after taking the capsule at 18 (41%) centres. Six centres indicated that people were instructed to resume a normal diet 24-48 hours after treatment, but a LID inpatient menu was not provided. Compliance with the LID advice was assessed in 26 (59%) centres, although all except one used a simple verbal check rather than a formal dietary assessment. None of the centres reported measuring iodine status and only two clinicians said their centre would delay treatment if someone said they had not followed a LID.

Thirty-one of the 56 clinicians (53%) indicated that they thought people coped very well with the diet, although free text comments indicated that some groups of people were more likely to find the diet difficult, specifically, people with diabetes, vegans/vegetarians, older people and people from non-British backgrounds. The diet was identified as being a source of anxiety for some people, and there were comments that some people were more restrictive than advised and attempted to follow no-iodine diets, rather than reduced iodine. However, clinicians also said that there were people who liked feeling in control of a part of their cancer treatment, and who experienced other health benefits from thinking about what they were eating. The UK LID-WG diet sheet was highlighted as making advice clearer and easier to follow.

Two clinicians (a clinical nurse specialist and an oncologist) thought that people did not cope with the diet but provided no specific comments, and one oncologist reported not asking about the diet because they didn't think there was good evidence for efficacy so it didn't matter if people followed it or not.

Discussion

This study gives information about clinical practice regarding low iodine diets prior to RIA for thyroid cancer in the UK since the introduction of the UK LID-WG diet sheet(16). The response rate was good with very good coverage across the regions of the UK, including all the devolved nations. Most centres advise a 14-day LID but there were variations regarding the advice given between centres. Overall, there was good awareness and usage of the UK LID-WG diet sheet and only four centres indicated that they were unaware of it. A further four said that they disagreed with some of the information in the sheet.

Variations in practice are perhaps unsurprising given the lack of clear evidence that following a LID or reducing UIC improves ablation success(6, 8). Of the four centres that reported not routinely advising a LID, only one large centre explicitly stated that they did not think the evidence was good enough. However, adherence to the diet was either not assessed at all or assessed by a simple question by most clinicians and only two indicated that treatment would be delayed if people reported that they did not follow a LID. This may reflect either a widespread lack of belief that the diet is necessary, as stated by one clinician, or a lack of confidence in ability to assess diet. None of the centres assessed iodine status using urinary iodine measurements, again perhaps unsurprising given concerns over inaccuracies in determining iodine status from UIC(17).

There appears to be most disagreement in practice about when people should restart a normal diet following RIA. Twenty-five of the 56 clinicians who answered the survey reported that they advised people to continue with dietary restriction 24-48 hours after RIA and six indicated that the LID was stopped after post-therapy whole body scan (Px-WBS), presumably to ensure good uptake of ^{131}I. Although we did not ask each centre to report when the Px-WBS occurred, it is carried out when residual activity permits imaging, typically around 2-10 days after RIA(5). Studies that examine whether advice to follow a LID improves ablation success report asking people to follow a LID prior to RIA but did not appear to ask people to continue after ^{131}I has been administered(9-11, 13), unless a Px-WBS was carried out(12). To our knowledge, no studies have assessed whether continuing a LID beyond the administration of RIA confers any benefit on outcomes, or what effect resuming a usual diet has on iodine status in this immediate post-treatment period.

As a survey of practice, our study did not capture what patients think of the LID. Over half of clinicians (53%) indicated that people coped very well with the diet, although some suggested that there are groups of people who struggle and that some people attempt to follow a very restrictive no-iodine diet. Two studies, both conducted in Korea, reported that people believed the LID to be important but found it difficult to follow because they enjoyed foods high in iodine, struggled to find alternatives and found it difficult to eat outside the home(18, 19). Difficulties with food eaten outside of the home were also reported by people in Brazil(20). Experiences may be different in the UK since the typical Korean diet is very high in iodine(21) and, in Brazil salt is iodized(20). However, there was anecdotal evidence that people in the UK found LID advice confusing and difficult to follow before the UK LID-WG released the standardised diet sheet(15). Clinicians in the current survey indicated that the standardised diet sheet has improved advice, but questions from people about the LID are still frequently posted on on-line forums(22).This is perhaps because there is potential for confusion if people find on-line advice from countries where salt is iodized (e.g., the USA) unlike the UK.

This study is the most comprehensive overview of UK practice regarding advice on the LID prior to RIA for thyroid cancer to date but there are some limitations. Despite good coverage, it is likely that not all UK centres have taken part. It is also possible that the clinician who completed the survey may not have been the one who knew most about practice regarding the LID in their centre, despite the initial recipient being asked to forward it to a more appropriate person if they felt they were unable to answer the questions. Overall, however, we are confident that this study is broadly representative of current UK practice regarding LID advice prior to RIA therapy for thyroid cancer.

We found evidence that the UK LID-WG diet sheet is recognised, used and has improved practice. Most UK practice regarding the LID is in line with current guidelines but there are variations between centres and non-adherence to the diet does not usually delay RIA. This is, perhaps, due to lack of convincing evidence in the literature that the LID is necessary. There is a need for more research in this area and this study is a part of an ongoing work investigating the LID. We are currently conducting a multi-centre retrospective review of ablation success rates between UK centres giving different LID advice, a qualitative study exploring patient experiences with the LID and a mixed- methods review of the literature regarding the LID prior to RIA for thyroid cancer. However, since LID advice is widely given at present, UK practice could be improved with more detailed assessment of dietary compliance, and harmonisation of advice on when to restart a normal diet.

2491 words

Statements

Acknowledgment

We would like to thank all the clinicians who completed the survey.

Statement of ethics

Ethical approval was not required to conduct the study.

Disclosure statement

LM and IHS are members of the UK Low Iodine Diet Working Group. The remaining authors report no conflict of interest.

Funding sources

This study was funded by the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol. The views expressed are those of the authors and not necessarily those of the NIHR or the Department of Health and Social Care.

Author contributions

The study was conceived by all the authors. CE, GH and IHS drafted the survey which was tested and refined by all the other authors. CA, MB, CE, IHS and LM researched and finalised the list of sites and disseminated the survey. CE and CA analysed the results and CE wrote the first draft of the paper, which was commented upon by all other authors.

References

1. Smittenaar CR, Petersen KA, Stewart K, Moitt N. Cancer incidence and mortality projections in the UK until 2035. British Journal of Cancer. 2016;115(9):1147-55.
2. Cancer Research UK. Thyroid Cancer Incidence Statistics 2018 [Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/thyroid-cancer/incidence.
3. Luster M, Clarke SE, Dietlein M, Lassmann M, Lind P, Oyen WJ, et al. Guidelines for radioiodine therapy of differentiated thyroid cancer. European journal of nuclear medicine and molecular imaging. 2008;35(10):1941-59.
4. Tuttle RM, Tala H, Shah J, Leboeuf R, Ghossein R, Gonen M, et al. Estimating risk of recurrence in differentiated thyroid cancer after total thyroidectomy and radioactive iodine remnant ablation: using response to therapy variables to modify the initial risk estimates predicted by the new American Thyroid Association staging system. Thyroid : official journal of the American Thyroid Association. 2010;20(12):1341-9.
5. Perros P, Boelaert K, Colley S, Evans C, Evans RM, Gerrard Ba G, et al. Guidelines for the management of thyroid cancer. Clinical Endocrinology. 2014;81:1-122.
6. Li JH, He ZH, Bansal V, Hennessey JV. Low iodine diet in differentiated thyroid cancer: a review. Clinical Endocrinology. 2016;84(1):3-12.
7. Miller R, Spiro A, Stanner S. Micronutrient status and intake in the UK – where might we be in 10 years' time? Nutrition Bulletin. 2016;41(1):14-41.
8. Sawka AM, Ibrahim-Zada I, Galacgac P, Tsang RW, Brierley JD, Ezzat S, et al. Dietary iodine restriction in preparation for radioactive iodine treatment or scanning in well-differentiated thyroid cancer: a systematic review. Thyroid. 2010;20(10):1129-38.
9. Pluijmen MJ, Eustatia-Rutten C, Goslings BM, Stokkel MP, Arias AM, Diamant M, et al. Effects of low-iodide diet on postsurgical radioiodide ablation therapy in patients with differentiated thyroid carcinoma. Clin Endocrinol (Oxf). 2003;58(4):428-35.

10. Sohn SY, Choi JY, Jang HW, Kim HJ, Jin SM, Kim SW, et al. Association between excessive urinary iodine excretion and failure of radioactive iodine thyroid ablation in patients with papillary thyroid cancer. Thyroid. 2013;23(6):741-7.
11. Morris LF, Wilder MS, Waxman AD, Braunstein GD. Reevaluation of the impact of a stringent low-iodine diet on ablation rates in radioiodine treatment of thyroid carcinoma. Thyroid. 2001;11(8):749-55.
12. Yoo ID, Kim SH, Seo YY, Oh JK, O JH, Chung SK. The success rate of initial (131)i ablation in differentiated thyroid cancer: comparison between less strict and very strict low iodine diets. Nuclear medicine and molecular imaging. 2012;46(1):34-40.
13. Lee M, Lee YK, Jeon TJ, Chang HS, Kim BW, Lee YS, et al. Low iodine diet for one week is sufficient for adequate preparation of high dose radioactive iodine ablation therapy of differentiated thyroid cancer patients in iodine-rich areas. Thyroid. 2014;24(8):1289-96.
14. Pacini F, Brianzoni E, Durante C, Elisei R, Ferdeghini M, Fugazzola L, et al. Recommendations for post-surgical thyroid ablation in differentiated thyroid cancer: a 2015 position statement of the Italian Society of Endocrinology. Journal of Endocrinological Investigation. 2016;39:341-7.
15. Prestwich RJ, Gerrard GE. Low-iodine diet before radioiodine uptake scans or therapy--flawed advice to U.K. patients. Clinical Oncology (Royal College of Radiologists). 2005;17(2):73-4.
16. UK Low Iodine Diet Working Group. The Low Iodine Diet 2018 [Available from: http://www.btf-thyroid.org/images/documents/Low_Iodine_Diet_Factsheet.pdf.
17. Ji C, Lu T, Dary O, Legetic B, Campbell NR, Cappuccio FP. Systematic review of studies evaluating urinary iodine concentration as a predictor of 24-hour urinary iodine excretion for estimating population iodine intake. Revista panamericana de salud publica = Pan American journal of public health. 2015;38(1):73-81.
18. Moon J-A, Yoo C-H, Kim MH, Lee SM, Oh YJ, Ryu YH, et al. Knowledge, Self-Efficacy, and Perceived Barriers on the Low-Iodine Diet among Thyroid Cancer Patients Preparing for Radioactive Iodine Therapy. Clinical nutrition research. 2012;1(1):13-22.
19. Lee KJ, Chang SO, Jung KY. Experiences with a low-iodine diet: A qualitative study of patients with thyroid cancer receiving radioactive iodine therapy. European Journal of Oncology Nursing. 2016;23:43-50.
20. Padovani RP, Maciel RMB, Kasamatsu TS, Freitas BCG, Marone MMS, Camacho CP, et al. Assessment of the Effect of Two Distinct Restricted Iodine Diet Durations on Urinary Iodine Levels (Collected over 24 h or as a Single-Spot Urinary Sample) and Na(+)/I(-) Symporter Expression. European Thyroid Journal. 2015;4(2):99-105.
21. Kim HI, Oh H-K, Park SY, Jang HW, Shin M-H, Kim SW, et al. Urinary iodine concentration and thyroid hormones: Korea National Health and Nutrition Examination Survey 2013–2015. 2019;58(1):233-40.
22. Unknown. Thyroid Cancer Group. Thyroid Cancer. UK: MacMillan Cancer Support; 2019.

Tables

Table 1. Regional responses

Table 2. Summary of survey answers for 44 centres advising a low iodine diet prior to radioiodine ablation.

Supplement: UK Low Iodine Diet Sheet; UK Low Iodine Diet Working Group Supporting Documents; survey items and possible response options